#### (19) World Intellectual Property **Organization** International Bureau





(43) International Publication Date 8 July 2004 (08.07.2004)

PCT

#### (10) International Publication Number WO 2004/057025 A3

(51) International Patent Classification7:

C12Q 1/68

(21) International Application Number:

PCT/EP2003/014813

(22) International Filing Date:

22 December 2003 (22.12.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: PCT/EP02/14877

20 December 2002 (20.12.2002)

- (71) Applicant (for all designated States except US): BIODE-TECTION SYSTEMS B.V. [NL/NL]; Badhuisweg 3, NL-1031 CM Amsterdam (NL).
- (72) Inventors; and
- Inventors/Applicants (for US only): VAN DER BURG, Bart [NL/NL]; Tuurdijk 17, NL-3997 MS 't Goy (NL). SONNEVELD, Edwin [NL/NL]; Etta Palmstraat 34, NL-2135 LE Hoofddorp (NL). BROUWER, Abraham [NL/NL]; Gang 14, NL-2242 KD Wassenaar (NL).
- (74) Agent: VERNOUT, Robert; Arnold & Siedsma, Sweelinckplein 1, NL-2517 GK Den Haag (NL).

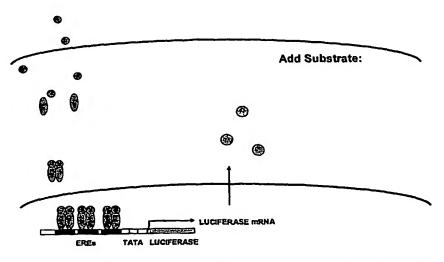
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 5 August 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR DETERMINING THE PRESENCE OF ONE OR MORE LIGANDS IN A SAMPLE



(57) Abstract: The present invention relates to a method for determining the presence of one or more specific ligands in a sample, said method comprising; a) contacting the sample with an array of cell lines, each cell line comprising a reporter gene construct responding to a cellular pathway which is induced by a different specific ligand; b) measuring the activity of the reporter gene in the individual cell lines; c) comparing the measured activity in the individual cell lines; and d) determining the presence of the ligands in the sample based on said comparison.



Interponal Application No PCT/EP 03/14813

A. CLASSIF	FICATION OF SUBJECT MATTER C12Q1/68						
110 /							
B. FIELDS	International Patent Classification (IPC) or to both national classifica	lion and if O					
Minimum do	cumentation searched (classification system followed by classification	n symbols)					
IPC 7	C12Q						
		the decrease and helydod in the fields on	orchod				
Documentati	ion searched other than minimum documentation to the extent that so	ich documents are included in the heids se	aicheu				
Electronic da	ata base consulted during the international search (name of data bas	se and, where practical, search terms used	)				
	ternal, BIOSIS, EMBASE, WPI Data						
	,						
			·				
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT						
Category °	Citation of document, with indication, where appropriate, of the rek	evant passages	Relevant to daim No.				
, <u>, , , , , , , , , , , , , , , , , , </u>	OUASDAGKSDO M S ST AL		1–17				
X,Y	QUAEDACKERS M E ET AL:   "4-hydroxytamoxifen trans-repress	es	1-17				
	nuclear factor-kappa B activity i	n human					
	osteoblastic U2-OS cells through						
ļ	receptor (ER)alpha, and not throubeta."	ign EK					
	ENDOCRINOLOGY. MAR 2001,						
	vol. 142, no. 3, March 2001 (2001	L-03),					
	pages 1156-1166, XP0001180339 ISSN: 0013-7227						
	abstract						
	page 1157, right-hand column - pa	age 1158,					
	left-hand column page 1160, left-hand column; figu	res 1-5					
	•	-/- <del>-</del>					
1							
<u> </u>	<u> </u>						
X Furt	ther documents are listed in the continuation of box C.	Patent family members are listed	in annex.				
	ategories of cited documents:	"I later document published after the Int	ernational filing date n the application but				
"A" docum	'A' document defining the general state of the art which is not considered to be of particular relevance on sidered to be of particular relevance on the considered to be of t						
'E' earlier	document but published on or after the International date	"X" document of particular relevance; the cannot be considered novel or cannot	ot be considered to				
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention							
cliation or other special reason (as specified)  cannot be considered to involve an inventive step when the document referring to an oral disclosure use, exhibition or document is combined with one or more other such document.							
other means other means  "P" document published prior to the international filling date but							
tater	than the priority date claimed	& document member of the same patent family					
Date of the	Date of the actual completion of the international search  Date of mailing of the international search report						
	13 April 2004	14/06/2004					
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2	Authorized officer					
	NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	Lohon T					
1	Fax: (+31-70) 340-3016	Leber, T					

Intomional Application No
PCT/EP 03/14813

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	<u> </u>
egory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
,Υ	GRAD J M ET AL: "The androgen receptor (AR) amino-terminus imposes androgen-specific regulation of AR gene expression via an exonic enhancer." ENDOCRINOLOGY. MAR 2001, vol. 142, no. 3, March 2001 (2001-03), pages 1107-1116, XP0001180513 ISSN: 0013-7227 page 1108, right-hand column - left-hand column figures 4,5	1-17
΄,Υ	ROGATSKY I ET AL: "Factor recruitment and TIF2/GRIP1 corepressor activity at a collagenase-3 response element that mediates regulation by phorbol esters and hormones."  THE EMBO JOURNAL. 1 NOV 2001, vol. 20, no. 21, 1 November 2001 (2001-11-01), pages 6071-6083, XP0001180511 ISSN: 0261-4189 page 6080, left-hand column - page 6081, left-hand column figures 1,2,4,5	1-17
•	BEATO M: "GENE REGULATION BY STEROID HORMONES" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 56, no. 3, 10 February 1989 (1989-02-10), pages 335-344, XP000051659 ISSN: 0092-8674 page 336; figure 2	9,13
Y	LEGLER J ET AL: "Development of a stably transfected estrogen receptor-mediated luciferase reporter gene assay in the human T47D breast cancer cell line." TOXICOLOGICAL SCIENCES: AN OFFICIAL JOURNAL OF THE SOCIETY OF TOXICOLOGY. MAR 1999, vol. 48, no. 1, March 1999 (1999-03), pages 55-66, XP0009028295 ISSN: 1096-6080 page 64, left-hand column	11,12
Υ	US 2002/137019 A1 (MARKUS STEVEN ET AL) 26 September 2002 (2002-09-26) paragraphs '0163! - '0164!; figure 12	11,12
A	US 6 103 479 A (TAYLOR D LANSING) 15 August 2000 (2000-08-15)	

Intensional Application No
PCT/EP 03/14813

		PCT/EP 0	3/14813
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	<del>"</del>	Relevant to claim No.
A	WILSON VICKIE S ET AL: "A novel cell line, MDA-kb2, that stably expresses an androgen- and glucocorticoid-responsive reporter for the detection of hormone receptor agonists and antagonists." TOXICOLOGICAL SCIENCES: AN OFFICIAL JOURNAL OF THE SOCIETY OF TOXICOLOGY. MAR 2002, vol. 66, no. 1, March 2002 (2002-03), pages 69-81, XP0009028294 ISSN: 1096-6080		

Information on patent family members

Interional Application No
PCT/EP 03/14813

	atent document d in search report		Publication date		Patent family member(s)		Publication date
US	2002137019	A1	26-09-2002	AU WO	4940101 0172332		08-10-2001 04-10-2001
US	6103479	A	15-08-2000	US AU CA CA EP JP WS US US US US AU CA EP JP	5989835 730100 6667898 2282658 2410688 0983498 2000509827 2002355090 9838490 6548263 6671624 2003096322 6620591 2004009539 6416959 6573039 2004063162 734704 3297197 2257287 0912892 2000512009	A B2 A A1 A1 A1 B1 B1 B1 B1 B1 B1 B1 B1 B1 B1	23-11-1999 22-02-2001 18-09-1998 03-09-1998 03-09-1998 08-03-2000 02-08-2000 10-12-2002 03-09-1998 15-04-2003 22-05-2003 16-09-2003 15-01-2004 09-07-2002 03-06-2003 01-04-2004 21-06-2001 05-01-1998 04-12-1997 06-05-1999 12-09-2000
				WO	9745730 	WT	04-12-1997